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Original Article

CLINICAL EVALUATION OF POTENTIAL ANTI-INFLAMMATORY EFFECT OF VITAMIN D3 ADJUVANT THERAPY FOR CHRONIC ASTHMA IN IRAQI PATIENTS

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ABSTRACT

Objective: This study was designed to evaluate the potential anti-inflammatory effect of vitamin D_3 supplementation in Iraqi patients with chronic asthma.

Methods: Forty-four candidate patients were diagnosed with asthma during their visit to hospital allocated as 20 patients assigned to receive conventional therapy for asthma and 24 patients assigned to receive conventional therapy for asthma plus 2000 I. U vitamin D_3 tablet for three months period. Also, 30 apparently healthy subjects were included in the study as a control group. Pulmonary function test, serum 25-OH vitamin D levels, serum Interlukin-10 (IL-10) levels, serum tumor necrosis factor alpha (TNF-α) levels were measured before and after three months therapy.

Results: After three months treatment, there was a highly significant improvement in both measured and percentage of predicted value of pulmonary function test (PFT) compared to the pre-treatment value for both group 1 and group 2 patients ($p<0.01$). Also, a highly significant increase in total endogenous vitamin D level in group 2 when compared to group 1 patients after three months period ($p<0.01$). Group 2 patients presented with a significant increase in mean IL-10 after three months of treatment when compared to pre-treatment level ($p<0.05$). The mean TNF-α level was increased non-significantly in both study groups, but the higher level was found in group 1 patients than in group 2 patients when compared to pre-treatment level ($p>0.05$).

Conclusion: There was a significant increase in the level of anti-inflammatory biomarker interleukin-10 (IL-10), though no clear effect on tumor necrosis factor-α (TNF-α) was noticed after three months treatment with vitamin D_3 supplementation.

Keywords: Asthma, Endogenous vitamin D_3, Pulmonary function test, Anti-Inflammatory markers

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INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role especially, mast cells, neutrophils, eosinophils, T lymphocytes, macrophages, and epithelial cells [1]. Asthma is usually associated with chronic inflammation of the mucosa from the trachea to terminal bronchioles but with a predominance in the bronchi (cartilaginous airways) [2]. Macrophage has the capacity to initiate inflammatory response via the release of a certain type of cytokines but can also release anti-inflammatory mediators, such as interleukin-10 (IL-10), which its secretion is reduced in alveolar macrophages of asthmatic patients [3].

Dendritic cells are specialised cells that have a unique ability to induce a T-lymphocyte mediated immune response and therefore play a critical role in the development of asthma [4]. Immature dendritic cells promote T helper 2 (TH2) cell differentiation and require cytokines, such as interleukin-12 (IL-12) and tumour necrosis factor α (TNF-α), to promote the normally predominant T helper-1 (TH1) response in the respiratory tract [4]. Vitamin D is an essential nutrient that is usually obtained through exposure to sunlight, and secondarily through diet and dietary supplements [5]. Vitamin D receptors (VDR) containing cells are targets for vitamin D activity [6], one of the superfamily of nuclear receptors [7], which is a critical molecule in calcium metabolism, bone turnover, and other immune and inflammatory disorders [8].

Vitamin D receptor in the lung have been proven to be fully functional when 25(OH)D is converted into active form $1,25(OH)_2D$ in respiratory epithelial cells where increased synthesis of both VDR and CYP24A1 (a hydroxylase that metabolizes 1,25(OH)D) in bronchial smooth muscle cells has been recognized [9]. It is now well known that in the human body CYP27B1 and VDR are presented in cells involved in the immune/inflammation system which provides the biological mechanism of vitamin D in inflammatory diseases [10].

In macrophages, the active form of vitamin D ($1,25(OH)_2D_3$) cause a reduction of gene expression and protein release of pro-inflammatory mediators, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and monocyte chemo attractant protein-1 (MCP-1), result in reduction of monocytes/macrophages recruitment and overall inflammation within tissue [11-13].

Vitamin D deficiency lower steroid-induced production of IL-10 and decreasing the anti-inflammatory activity of glucocorticoids while vitamin D supplementation reverses steroid resistance [14]. Nevertheless, vitamin D oral supplementation for 7 d in steroid-refractory patients with asthma restored the dexamethasone induction of IL-10 [15].

Accordingly, this study was designed to evaluate the potential anti-inflammatory effect of vitamin D_3 supplementation on the level of pro-inflammatory mediator tumor necrosis factor-α (TNF-α) and anti-inflammatory cytokine interleukin-10 (IL-10) in Iraqi patients with chronic asthma.

MATERIALS AND METHODS

Study design

This is a prospective randomised controlled open-label interventional study to evaluate the anti-inflammatory effect of vitamin D_3 in asthma patients.

Patients

Forty-four candidate patients were diagnosed with asthma during their visit to the hospital. The patients were under the supervision of

a pulmonary specialist and were treated according to clinical practice guideline and disease severity.

The local clinical research ethics committee, in accordance with Helsinki declaration 1998, approved the study protocol and all subjects gave written informed consent to participate in the study. The eligible patients and subjects were allocated into three main groups:

Group 1: Include 20 patients who have diagnosed with asthma are assigned to receive conventional therapy for asthma according to disease stage and severity for three months period.

Group 2: Include 24 patients who have diagnosed with asthma are assigned to receive conventional therapy for asthma according to disease stage and severity plus 2000 I. U vitamin D_3 fast dissolve mini tablet (Natrol, USA) for three months period.

Control group: Include 30 apparently healthy control subjects.

Material and methods

- **Pulmonary function test (PFT) using spirometry**

It was measured using Spiro Air (volumetric P. F. T), (Medisoft, Belgium) in which forced vital capacity (FVC), forced expiratory volume in one second (FEV1), peak expiratory flow (PEF) both the measured and percentage of predicted value in addition to forced expiratory volume in one second/forced vital capacity (FEV1/FVC) ratio were measured before and after three months therapy for both group 1 and group 2 patients.

- **Specimens collection**

Five millilitre of venous blood were drawn using a plastic disposable syringe and collected in the plain disposable tube (gel and clot activator) and was allowed to clot and separated by centrifuge at a speed of 3000 rpm for 10 min. The serum samples were stored at (-40 °C) until the time of examination.

- **Serum 25-OH vitamin D level measurement**

It was determined using commercial enzyme-linked immune-sorbent assay (ELISA) kit (Euroimmun, Germany), measured at baseline in group 1, group 2 patients and healthy control groups and after three months treatment in group 1 and group 2 patients.

- **Serum Interleukin-10 (IL-10), Tumor necrosis factor-α (TNF-α) level measurement**

It was determined using commercial enzyme-linked immunosorbent assay (ELISA) kit (Elabscience Biotechnology, China) measured before and after three months therapy for both groups 1 and group 2 patients.

- **Body mass index (BMI) measurement**

Body Mass Index (BMI) is an individual weight in kilogrammes divided by the square of their height in meters (kg/m2).

Statistical analysis

The Statistical Analysis System Minitab 16.1 (2010) were used. Data presented as (mean±SD). Pearson Chi-square test was utilized to detect significant differences among demographic variables, while paired *t*-test was used to compare between pre-and post-treatment results, two sample *t*-test used to compare pre or post treatment between group 1 and 2. Analysis of Variance (ANOVA) was utilized to compare between the studied parameters among different patient groups.

NS: no significant differences ($p>0.05$), (*) significant difference ($p<0.05$), (**) highly Significant difference ($p<0.01$).

RESULTS

Patients demographic and disease characteristics

Table 1 demonstrates the patient demographic and disease characteristic for 74 subjects including 53 female (71.6%) and 21 male genders (28.4%) with no significant statistical difference was found among study groups in respect to both genders ($p>0.05$).

The age range for the groups where between 14-71 y with the mean age of the study groups were as follows: group1 patients (40.75±17.31) years, and group 2 patients (41.4±13.6) years, control group (45.86±15.83) years with no significant statistical difference was found among study groups in respect to age ($p>0.05$).

Positive family history of asthma was found in (65%) and (58.3%) of group 1 and group 2 patients respectively while negative family history was found in (35%) and (41.7%) for group 1 and group 2 patients respectively with no significant statistical difference between these groups ($p>0.05$). Considering the patient's residence there were (85%) of group1 patients versus (79.2%) of group 2 patients were urban, and (15%) of group 1 patients versus (20.8%) of group 2 patients were rural with no significant statistical difference between both groups ($p>0.05$).

The duration of the disease for group 1 and group 2 patients respectively were as follows: (80%) versus (62.5%) for less than 20 y, (15%) versus (25%) for (21-40) years duration, (5%) versus (12.5%) for (41-60) years duration, with a mean of (12.8±11.2) years for group 1 patients and (20.2±15.4) years for group 2 patients respectively and no significant statistical difference was found between both groups in respect to duration of the disease ($p>0.05$).

The mean body mass index (BMI) for group 1 patients was (33.20±8.54) kg/m^2 and (29.25±7.44) kg/m^2 for group 2 patients with no significant statistical difference was found between study groups in respect to the BMI ($p>0.05$).

Table 1: Patients demographic and disease characteristics

Variable	Study groups			
	Group 1	Group 2	Control group	*P* value
Age (year)	40.75±17.31^{aNS}	41.4±13.6^{aNS}	45.86±15.83	0.890^{bNS}
BMI(kg/m^2)	33.20±8.54	29.25±7.44	-------	0.114^{NS}
Gender	n(%)	n(%)	n(%)	
Female	13(65.0)	20(83.3)	20(66.7)	0.299^{NS}
Male	7(35.0)	4(16.7)	10(33.3)	
Total	20(100)	24(100)	30(100)	
Family history	n(%)	n(%)	n(%)	0.651^{NS}
Positive	13(65.0)	14(58.3)	-------	
Negative	7(35.0)	10(41.7)	-------	
Residence	n(%)	n(%)	n(%)	0.617^{NS}
Urban	17(85.0)	19(79.2)	-------	
Rural	3(15.0)	5(20.8)	-------	
Duration of the disease (year)	n(%)	n(%)	n(%)	0.072^{NS}
≤20	16(80.0)	15(62.5)	-------	
21-40	3(15.0)	6(25.0)	-------	
41-60	1(5.0)	3(12.5)	-------	
≥ 61	None	None	-------	

Data presented as mean±SD, a number of patients (n) and percentage (%), a: comparison with control group, b: comparison between group 1 and 2, NS: no significant differences ($p>0.05$).

Effect of conventional therapy alone and in combination with vitamin D_3 supplement on pulmonary function test (PFT), (spirometry) in asthmatic patients

The mean forced vital capacity (FVC), mean forced expiratory volume in one second (FEV1), and mean peak expiratory flow (PEF) both the measured and the percentage of predicted value showed no significant difference at baseline and after three months between the study groups (1,2) (p>0.05) while highly significant increase was noticed after three months treatment compared to pre-treatment value for both group 1 and group 2 patients (p<0.01).

The mean forced expiratory volume in one second/forced vital capacity (FEV1/FVC) ratio showed a significant difference at baseline level between group 1 and group 2 (p<0.05), but no significant differences was found after three months between both groups (p>0.05). There was no significant increase in (FEV1/FVC) ratio after three months in group 1 when compared to pre-treatment value (p>0.05), nevertheless, group 2 showed a highly significant increase after three months treatment compared to pre-treatment value (p<0.01) as shown in table 2.

Effect of conventional therapy alone and in combination with vitamin D_3 supplement on total endogenous vitamin D level in asthmatic patients

Table 3 showed that at the baseline (pre-treatment) mean level of endogenous vitamin D showed no significant differences when comparing group 1 with control and group 2 (p>0.05), meanwhile a highly significant difference was between group 2 and control group (p<0.01). Following treatment for three months, there was highly significant increase in endogenous vitamin D level in group 2 when compared to group 1 patients (p<0.01). A highly significant increase in endogenous vitamin D level post-treatment was found in both study groups 1 and 2 compared to pre-treatment level (p<0.01).

Table 2: Effect of conventional therapy alone and in combination with vitamin D_3 supplement on pulmonary function test (PFT) (spirometry) in asthmatic patients treated for three months

Variable	Study groups		
FVC(L) Meas.	Group1	Group 2	*P* value
Pre-treatment	2.113±1.075	1.840±0.583	0.317^{NS}
Post-treatment	2.655±1.107	2.415±0.733	0.414^{NS}
P-value	0.000**	0.000**	-------
FVC(%Pred. Val.)	Group1	Group 2	*P* value
Pre-treatment	58.60±17.97	57.33±17.71	0.816^{NS}
Post-treatment	75.15±12.52	74.04±18.55	0.815^{NS}
P-value	0.000**	0.000**	-------
FEV1(L) Meas.	Group1	Group 2	*P* value
Pre-treatment	1.584±0.871	1.189±0.514	0.084^{NS}
Post-treatment	2.091±1.013	1.753±0.674	0.212^{NS}
P-value	0.009**	0.000**	-------
FEV1(%Pred. Val.)	Group1	Group 2	*P* value
Pre-treatment	50.90±16.04	43.92±20.36	0.210^{NS}
Post-treatment	68.85±14.93	63.04±20.68	0.287^{NS}
P-value	0.003**	0.000**	-------
FEV1/FVC(%)	Group1	Group 2	*P* value
Pre-treatment	74.37±13.25	63.62±14.33	0.013*
Post-treatment	78.30±12.58	71.45±13.15	0.086^{NS}
P-value	0.341^{NS}	0.005**	-------
PEF(L/S) Meas.	Group1	Group 2	*P* value
Pre-treatment	3.209±1.361	2.383±1.155	0.039*
Post-treatment	4.158±1.557	3.422±1.496	0.120^{NS}
P-value	0.007**	0.001**	-------
PEF (%Pred. Val.)	Group1	Group 2	*P* value
Pre-treatment	44.65±14.41	36.21±17.81	0.090^{NS}
Post-treatment	58.30±16.01	50.92±19.54	0.176^{NS}
P-value	0.001**	0.000**	-------

Data presented as mean±SD, FVC(L): forced vital capacity in liter,FEV1(L): forced expiratory volume in one second in liter, FEV1/FVC: forced expiratory volume in one second/forced vital capacity ratio, PEF(L/S): peak expiratory flow in liter per second, % Pred. Val.: percentage of predicted value, Meas.: measured value, NS: no significant differences (p>0.05),(*) significant difference (p<0.05),(**) highly significant difference (p<0.01).

Table 3: Effect of conventional therapy alone and in combination with vitamin D_3 supplement on total endogenous vitamin D level in asthmatic patients treated for three months

Variable	Study groups			
Endogenous Vitamin D (ng/ml)	Group 1	Group 2	Control group	*P* value
Pre-treatment	8.90 ± 6.82^{aNS}	$6.33\pm4.64^{a**}$	13.26±9.06	0.162^{bNS}
Post-treatment	12.59±7.08	23.25±8.73	-------	0.000^{**}
P-value	0.002^{**}	0.000^{**}	-------	-------

Data presented as mean±SD, Endogenous vitamin D measured as (25-OH vitamin D), a: comparison with control group, b: comparison between group 1 and group 2, NS: no significant differences (p>0.05), (**) highly significant difference (p<0.01).

Effect of conventional therapy alone and in combination with vitamin D_3 supplement on interleukin-10 (IL-10) and tumor necrosis factor alpha (TNF-α) level in asthmatic patients

Table 4 showed no significant difference of mean interleukin-10 (IL-10) level at the baseline and post-treatment between both study groups (1and 2) (p>0.05). After three months of treatment, group 1 patients had no significant increase in the mean IL-10 compared to pre-treatment level (p>0.05), while in group 2 patients there was a significant increase in mean IL-10 after three-month treatment compared to pre-treatment level (p<0.05).

On the other hand, at the baseline, there was a significant difference in mean level of tumor necrosis factor alpha (TNF-α) between group 1 and group 2 patients (p<0.05) but no significant differences was seen post-treatment between both study groups (p>0.05). After three months of treatment, the mean TNF-α level was increased non-significantly in both study groups, but the higher level was found in group 1 patients than in group 2 patients when compared to pre-treatment level (p>0.05).

Table 4: Effect of conventional therapy alone and in combination with vitamin D_3 supplement on interleukin-10 (IL-10) and tumor necrosis factor alpha (TNF-α) level in asthmatic patients treated for three months

Variable	Study groups		
IL-10 (pg/ml)	Group 1	Group 2	*P* value
Pre-treatment	29.5±5.17	37.0±8.64	0.460^{NS}
Post-treatment	43.4±11.49	73.1±16.89	0.156^{NS}
P-value	0.281^{NS}	0.029^{*}	-------
TNF-α (pg/ml)	Group 1	Group 2	*P* value
Pre-treatment	23.5±5.74	44.9±7.82	0.033^{*}
Post-treatment	48.9±22.14	48.4±11.88	0.985^{NS}
P-value	0.202^{NS}	0.750^{NS}	-------

Data presented as mean**±**SD**,** NS: no significant differences (p>0.05),(*) significant difference (p<0.05),(**) highly significant difference (p<0.01).

DISCUSSION

Approximately 5–15% of patients with asthma symptoms and exacerbation are uncontrolled despite of routine controller medications including corticosteroids [16]. Part of this variability may be explained by endogenous vitamin D levels; some studies suggested that vitamin D may enhance the effects of inhaled corticosteroids [16-18]. Vitamin D might protect against inflammatory reactions to environmental pollutants and might be broadly important in regulating chronic inflammation of the lung [19]. Nutrition has represented an important conditioning factor of many chronic diseases with many studies explore the role of adjuvant therapy in the treatment of asthma-like antioxidant vitamins, trace elements [20], and essential oils like gamma linoleic acid [21,22]. Up to the best knowledge, there is no clinical study reported for Iraqi adult population to explore the role of vitamin D_3 supplement in asthma. Thus, the present study was undertaken to clinically evaluate whether or not vitamin D_3 can improve pulmonary function and health-related quality of life in asthmatic patients concomitantly with reduction of inflammatory and oxidative burden in those patients.

In the present study, both genders were enrolled in the study with a slight predominance of female over the male in both study groups (3:1). This was consistent with another previous study since adult females are more severely affected by asthma and raise the possibility that hormonal or biochemical differences related to sex might play a role in the pathophysiology of asthma [23].

Positive family history to asthma was found in more than (50%) in both groups of the present study. Al-Kubaisy *et al.* in 2004 studied the effect of family history among asthmatic primary school children and noticed that child of asthmatic father, mother or sibling were higher rate and considered a significant risk factor for having asthma by their index child [24]. These results were supported by another study were asthma are highest among those who had more than one first-degree relative with asthma and identify sex-specific differences in the risk of asthma in relation to heredity factor [25].

Most of the asthmatic patients enrolled in this study were resident in urban rather than rural area, and were more prone to be exposed to ambient air pollution [26]. High levels of vehicle emissions, westernised lifestyle, with increasing indoor allergens exposure such as house dust mite and animal dander all may explain differences in asthma prevalence and morbidity among adults in urban versus rural areas [24,27].

Epidemiological studies worldwide allowed such explanations, in Rwanda, Musafiri *et al.* investigated the prevalence of atopy and asthma between urban and rural area, higher prevalence of asthma was found in the urban area [28]. Inversely, in New Zealand, the rate of asthma hospitalisation was higher in rural areas than in urban areas [29]. The possible explanation for the diversity is the fact that most people have different lifestyles and cultures, in addition to different environmental and genetic backgrounds [27].

With reference to the results in the present study, highly significant increase in both measured and percentage of predicted value in forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and peak expiratory flow (PEF) in both study groups after three months treatment when compared to pre-treatment value suggesting that this improvement was due to conventional therapy rather the effect of vitamin D_3 supplementation. On the other hand highly significant increase in the ratio of forced expiratory volume in one second/forced vital capacity (FEV1/FVC) in group 2 after three months treatment with vitamin D_3 supplementation when compared to group 1, (p<0.01). Columbo *et al.* (2014) found no significant association between serum vitamin D and spirometric values, and vitamin D was similar in subjects with lower FEV1% (<70%), also no variation in the spirometric values had been obtained after a 12 w treatment with 2000 IU vitamin D3 supplementation [30].

Additionally, Nageswari *et al.* (2014) investigated the addition of 1000 IU of vitamin D_3 to conventional therapy when compared to conventional therapy alone on pulmonary function test, he found that patients in both groups had a significant improvement in the percentage of predicted value of (FEV1) after three months treatment [31].

In the present study, asthmatic patients showed a significant decline in mean total endogenous vitamin D level compared to healthy controls. Following vitamin D supplementation, post treatment, highly significant increase in the mean of the total endogenous vitamin D level in both asthmatic groups when compared to pre-treatment level. These finding can be explained by the following point, first; in the present study, serum 25-OH vitamin D level was measured which is considered the best circulating biomarker of vitamin D metabolic status since it reflects total vitamin D from dietary intake and sunlight exposure as well as the conversion of vitamin D from adipose tissue in the liver [32], accordingly we can't estimate the active vitamin D acquired from sunlight exposure or diet. Second, a higher significant increase in the mean of endogenous vitamin D level in group 2 when compared to group 1 post treatment with vitamin D_3 supplement to conventional therapy provided a good estimation of the potential effect of vitamin D in asthma control. These findings are in agreement with Menon *et al.* who reported that highly significant elevation of mean vitamin D level in both control group (asthmatic patients received standard medication only) and study group (asthmatic patients received standard therapy along with oral vitamin D (1000 IU) for 8 w) [33]. The lowest value of serum vitamin D was found in severely exacerbated asthma patients in which vitamin D promotes steroid sensitivity in the body and can downregulate an inflammatory state via gene expression and cytokine production, consequently vitamin D deficiency could be associated with an inability to switch off the inflammatory state [34].

This study was interested in tracking the changes in inflammatory cascade following adjuvant vitamin D therapy in asthmatic patients. A significant increase of mean interleukin-10 (IL-10) level in group 2 patients was found after three months, meanwhile, group 1 showed no significant increase of this anti-inflammatory cytokine suggesting a potential role of vitamin D on its activation. Aldubi *et al.*(2015) found that Serum 25-hydroxyvitamin D levels were positively correlated to the anti-inflammatory cytokine IL-10 and linked between reduced IL-10 levels and lung function in children with severe asthma, partly be explained by hypovitaminosis [35]. Another finding showed a positive correlation between serum 25-hydroxyvitamin D level and Broncho alveolar lavage level of the anti-inflammatory cytokine interleukin (IL)-10 in severe resistant asthma in children [36]. Controversially, at the baseline Korn *et al.* found no link between serum vitamin D status and serum IL-10 concentrations (as IL-10 levels in patients with more severe and uncontrolled asthma did not differ from that in patients with mild/moderate or controlled/partly controlled asthma [37]. A finding previously noted by another researcher who found that the administration of vitamin D_3 to healthy individuals and steroid resistant asthmatic patients enhanced subsequent responsiveness to dexamethasone for induction of IL-10 suggested that vitamin D_3 could potentially increase the therapeutic response to glucocorticoids in steroid resistant patients [15].

Tumor necrosis factor alpha (TNF-α) is a critical pro-inflammatory cytokine that might play an important role in severe refractory disease [38]. Reduced vitamin D levels are associated with increased expression of TNF-α, suggesting that enhanced expression of this pro-inflammatory cytokine is a potential pathway by which reduced vitamin D levels could exert pro-inflammatory effects in asthma [39]. The present study found that TNF-α increased in both study groups (1 and 2) after three months treatment, but not significant. When comparing mean differences in TNF-α level, it can be recognised that minimum increase in group 2 compared to the higher increase in group 1. Longer duration of vitamin D_3 supplementation might be required to explore the effect clearly. It was proposed that to achieve optimal anti-inflammatory effects by vitamin D, it is important to maintain serum vitamin D levels of greater than (30 ng/ml) in the physiologic range [40,41]. Recent study showed that serum TNF-α in vitamin D deficiency patients with severe asthma exacerbation was significantly increased compared to that in vitamin D sufficient patients, suggested that vitamin D_3 is a potential anti-inflammatory agent by attenuating the generation of TNF-α, blocking reactive oxygen species generation, and nuclear factor (NFkB) activation pathways in lipopoly-saccharides (LPS) stimulated airway epithelial cells [42]. All these observations suggested that evaluation of serum vitamin D concentrations should be considered in adult patients with asthma that responds suboptimally to ICS, and they give a promising preventive strategy that vitamin D_3 supplementation could result in improvement of these phenotypic variables in the subset of subjects with asthma who are vitamin D deficient [43].

The present study has few limitation including small sample size with different disease severity which required to verify the findings, short duration of patient follow-up, as longer period may be required to explore good results. In addition to some missing data in respect to lifestyle details of asthmatic patients (vitamin D acquires through sunlight exposure or from diet) and inability to restore vitamin D to the normal level prior to the study in order to explore the actual effect of vitamin D_3 supplementation on asthma parameter rather than replace of deficiency.

CONCLUSION

In the present study, many promising preventive strategies emerged from the available results since vitamin D relatively improve pulmonary function in asthmatic patients concomitantly with reduction of inflammatory burden in those patients, suggesting that vitamin D plays effective role to be a good candidate as an adjuvant therapy. Further evaluation is needed to explore the potential effect of vitamin D supplementation in acute or chronic asthma after recovering hypovitaminosis and optimisation of endogenous vitamin D status.

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CONFLICT OF INTERESTS

Declared none

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